



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

09/699,679

10/30/2000

Evan C. Unger

UNGR-1598

8248

7590

04/22/2005

S. Maurice Valla
WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103

EXAMINER

SHARAREH, SHAHNAM J

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 04/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/699,679

Applicant(s)

UNGER ET AL.

Examiner

Shahnam Sharareh

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3,4,6-17,22-35 and 54, 60-61, 63-65 is/are pending in the application.
- 4a) Of the above claim(s) 12 and 13 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 54 and 60 is/are allowed.
- 6) ☒ Claim(s) 3,4,6-11,14-17, 22-35,61 and 63-65 is/are rejected.
- 7) ☒ Claim(s) 54 and 60 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 06, 2004 has been entered.

Claims 3-4, 6-17, 22-35, 54, 60-61, 63-65 are pending.

2. Applicant has made an election of Group XII in Paper No. 22B, filed on April 10, 2003. Applicant has also made an election of species wherein R1 is acyl of 18 carbons, R2 is H, R3 is alkylene, R4 is acyl of 18 carbons, P is PEG-3400 and T is a peptide having sequence CRGDC and further the two cysteines are linked together via a disulfide linkage. Claims 3-4, 6-11, 14-35 and 54, 60-61, 63-65 are directed to the elected species and thus are under consideration.

3. A search directed to the elected species was conducted. Claims 3-4, 6-11, 14-35 and 54, 60-61, 63-65 are found to be free of art to the extent that they read on the elected species. Accordingly, claim 54 and 60 are allowed.

4. The search is extended to include a subgenus of claim 17 wherein R1 and R4 are acyl groups of 19-23 carbons, R2 is a lower alkyl, R3 is an alkylene, P is a PEG hydrophilic polymer and T is a targeting ligand directed to GPIIbIIIa receptor such as RGD.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

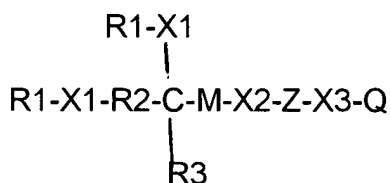
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 3, 4, 17, 6-11, 14, 22-35, 61, and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger et al WO 96/40285 ("WO '285").

The claims are directed to targeted vesicle compositions in aqueous carrier, gas filled liposomes comprising a phosphatidylcholine and a compound set forth in claim 17 wherein P is a hydrophilic polymer and T is targeting ligand that targets a receptor.

WO '285 teaches all elements of the compounds encompassed by the instant claims; namely the subgenus described above in paragraph 4. WO'285 teaches targeted vesicles comprising a gas, lipid structures containing phosphotidylcholine, and a compound having the formula:



The compositions of WO '285 meet the limitations of the instant claims. (see pages 61-63; page 124, lines 1-21; page 135, line 18-27; page 144, lines 14-30; page 156, line 1-14; claim 136-149, page 179-182; claim 164, page 183).

Examiner draws Applicant's attention to WO' 285 claim 135 at page 179 lines 13-15. The compound of page 179, meets the instant diamide structure. The carbon atom of this structure is linked to $\text{R}^2\text{-X}^1\text{-R}^1$ at one end, $\text{X}^1\text{-R}^1$ at the other, and R^3 at the 3rd position. The R^2 in WO '285 is defined as an alkylene moiety of 1-30 carbons encompassing the instantly claimed ethylene. X^1 can further be -NR^4 wherein R^4 is a hydrogen or alkyl. Such moiety meets the limitation of instant N-R^5 . Finally, R^1 of the WO '285 is an alkyl of 1-50 carbons, which reads on the instant R^4 and R^2 as acyl groups having 16-23 carbons. All other limitations are described in the below table as the corresponding groups. (see claim 136-149, page 179-182; claim 164, page 183).

Art Unit: 1617

Accordingly, when X^1 is NR^4 and R^4 is alkyl of 1-10 carbons, WO '285 teaches the subgenus of compounds that encompass compounds described as formula (IV) in the instant claim 17.

WO '285 also teaches that peptides such as RGD can be used as targeting agents. (see pages 50-54). In fact, the targeting agents taught by WO '285 can form cyclic disulfide bonds which meets the limitations of the instant claim 15. (see page 57, lines 23-30; page 58, line 1-page 60, line 20). WO' 285 also teaches targeted vesicles comprising liposomes comprising a phospholipid, a perfluorocarbon gas such as perfluorobutane, and a bioactive agent that can be incorporated into the targeted vesicles. The phospholipids employed by WO '284 include phosphatidylcholines such as dipalmitoylphosphatidylcholine (See page 29-30; page 90, lines 15-page 91, lines 11; page 108, lines 17-page 109, lines 32 examples 18-21, 37; claims 1-30; 170-185. Also see the table below).

Art Unit: 1617

The corresponding groups in the compositions of WO '285 are as follows:

Elemental groups of the Formula IV and the Instant Compositions	Rejected Species	Functional Group of the Compounds of WO '285 and the Compositional elements	Corresponding Subgenus	Citation
X1, X2	C=X3, C=X3-N(R8), -C=X3-N(R8)-C(=X3)-, wherein X3 is O or S	X2, X3	R5-X4-C(=X5)-, R5-C(=X5)-X4, -X4-C(=X5)-R5, R5-X4-C(=X5)-R5-C(=X5)-X4, wherein X1 is NR4, R3 is a H, R4 is an alkyl 1-10 carbons, R5 is a direct bond, X4 is O, NR4 or S, and X5 is O or S	Page 179, lines 15-22, 25-27. Page 180, lines 1-5
R1-N-R2 or R5-N-R4	R1=R4= acyl of 19-23, R2=R5=H or lower alkyl	X1	NR4, wherein R4 is H or lower alkyl	Page 179, lines 15. Page 180, lines 2-3
R3	Alkelene	R2	Alkelene of 1 to 30 carbons	Page 180, line 1
R1, R4	Acyl of 19-23 carbons	R1	Alkyl of 1-50 carbons	Page 179, line 27
P	Hydrophilic polymer is a polyalkyleneoxide	Z	Hydrophilic polymer, such as PEG, preferably having MW of about 2000-5000	Page 179, line 25. page 44, lines 1-6
T	Peptide directed to GPIIb/IIIa receptors	Q	Peptides directed to GPIIb/IIIa receptors such as RGD	Pages 50, 55-61, and page 179, line 26. page 183, line 13-15.
Vesicles	Gas filled Liposomes	Gas filled Liposomes	Gaseous Liposomes comprising phosphatidylcholine	Pages 83, lines 24-29, page 84, line 23-page 86, line 25; page 140, line 20-page 141, line 20; Examples page 167, lines 9-21; page 174, line 5-page 175, line 20.

WO'285 only lacks the explicit use of RGD via a PEG moiety with targeted vesicles comprising phosphatidylcholine and the claimed compound.

However, it would have been obvious to one of ordinary skill in the art at the time of invention to employ targeted vesicles of WO '285 with a PEG as a hydrophilic

Art Unit: 1617

polymer and link the targeting agent and a diamide structure within the scope of the instant claims, because as suggested by WO'285 patent itself, PEG moieties with average MW of 2000-5000 are suitable candidates for such purpose and they can be used for attaching to RGD.

The ordinary skill in the art would have had a reasonable expectation of success in preparing formulations with parameters instantly claimed, because WO'285 explicitly describes all such parameters. Therefore, the ordinary skill in the art would have had a reasonable expectation of success to employ them for their own intended use.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 17, 6-11, 14, 22-35 and 61, 63-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17, 61, 63 limit the functional groups R1, R3, R7 to "about" a specific number of carbons. Such limitation render the claim ambiguous because it is not clear for example what constitutes about 18 carbon atoms.

Allowable Subject Matter

Claims 54 and 60 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

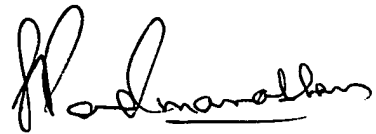
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SS


SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER